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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,289	08/21/2001	Samantha J. Busfield	MBIO1998-061CP1CN1(M)	9334

7590 05/23/2003

Millennium Pharmaceuticals, Inc.
75 Sidney Street
Cambridge, MA 02139

EXAMINER
MOSHER, MARY

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/934,289	Busfield
Examiner	**Art Unit**
Mosher	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *8/21/01, 3/11/03* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alignment*

DETAILED ACTION

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 28 and 29 are rejected under 35 U.S.C. 101 because the claims encompass products of nature. This rejection could be obviated by recitation of "isolated".

Claim Rejections - 35 USC § 112 2nd

Claims 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 23-25 are drawn to a polypeptide. The claim describes the polypeptide in terms of the degree of similarity (at least 95% identical) between its nucleic acid coding sequence and the SEQ ID NO:17 or the insert of ATCC 207173. This is confusing, because 63% of SEQ ID NO:17 is noncoding sequence, and one cannot tell from a polypeptide what the structure is for noncoding sequences which may flank the coding sequence. Therefore, a polypeptide could be 100% identical to the polypeptide encoded by SEQ ID NO:17, but be expressed from a nucleic acid about 40% identical to SEQ ID NO:17 (e.g., removing noncoding flanking sequences would decrease the nucleotide similarity to 63%, and changing 1/3 of the nucleotides using redundant codons would decrease the nucleotide similarity further to 42%). Is that 100% identical polypeptide encompassed by the claim, or not? Since the specification teaches only one peptide

encoded by the recited nucleic acids, and that peptide is SEQ ID NO:18, these claims have been treated as if they were drawn to a polypeptide comprising a sequence 95%, 98%, or 100% identical to SEQ ID NO:18. However, this treatment does not relieve applicant of the burden of response to this rejection.

Claims 32-34, 37 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 32 is drawn to a polypeptide defined by structure, which "exhibits a human TANGO-69 receptor activity." The specification speculates upon possible biological activities for a TANGO-69 receptor, but does not teach all the possible activities for the receptor. For example, the specification does not teach the function that the receptor serves in a normal (uninfected) human cell. Therefore it is not clear what is encompassed within "a human TANGO-69 receptor activity", and therefore unclear what polypeptides are encompassed by the claim. This affects the dependent claims.

Claims 27, 29, 33, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims depend from parent claims which recite a certain % identical to SEQ ID NO: 18. These dependent claims recite "further comprising an amino acid sequence which is [a larger %] identical..." Read literally, the dependent claims require two sequences in tandem. Is this really the intent? In the interest of compact prosecution, these dependent claims have been treated as if they said "wherein the amino acid sequence is [a larger

%] identical..." instead of "further comprising an amino acid sequence...." However, this treatment does not relieve applicant of the burden of response to this rejection.

Claim Rejections - 35 USC § 112 1st, description

Claims 28, 29, 30-34, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, not an enablement rejection. There are two aspects of this rejection, one involving "naturally occurring allelic variant" and one involving "a human TANGO-69-receptor activity".

Claims 28 and 29 involve a polypeptide, varying up to 2% or 5% from SEQ ID NO:18, which is a naturally occurring allelic variant. The specification discloses only one allele within the scope of the genus: SEQ ID NO:18. The specification proposes to discover other members of the genus by using a hybridization and sequencing procedure. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO: 1 relates to the structure of different alleles. In addition, according to the standard definition, the genus includes members that would be expected to have widely divergent functional properties. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of other unknown alleles having concordant or discordant functions. The common attributes of the genus are not described and the identifying attributes of individual alleles, other than SEQ ID NO:18, are not described. The nature of alleles

is that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

Claims 30-34, 37, and 38 involve polypeptides, varying up to 7.7%, 10%, 15%, or 20% from SEQ ID NO: 18, which "exhibit a human TANGO-69-receptor activity". As discussed above, the specification speculates upon possible biological activities for a TANGO-69 receptor, but does not teach all the possible activities for the receptor. For example, the specification does not teach the function that the receptor serves in a normal (uninfected) human cell. Therefore it is not clear what is encompassed within "a human TANGO-69 receptor activity". If the specification does not reasonably convey possession of the knowledge of the full scope of TANGO-69 receptor activities, logically it cannot convey possession of the full scope of protein variants which retain the undefined activities. Furthermore, the specification provides no guidance as to what regions of the protein structure are necessary for any of the protein's activities. Therefore, it is concluded that the specification does not reasonably convey possession of the full scope of the claimed variants with "a human TANGO-69-receptor activity".

Claim Rejections - 35 USC § 112 1st, enablement

Claims 23, 24, 26-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for variants of SEQ ID NO:18 which are able to interfere with

the ability of LIGHT/TANGO-69, LT.alpha., or HSV gD to bind mHVEM, does not reasonably provide enablement for all variants, or variants with any "TANGO-69-receptor activity." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches that soluble variants of HVEM "play a role analogous to other soluble members of the TNFR superfamily by interfering with the ability of LIGHT/TANGO-69 and LT.alpha. to bind mHVEM." This reasonably suggests how to use the variants which have this biological activity. The specification speculates upon other possible biological activities of TANGO-69 receptor(s). However, considering that the proteins fall into the TNFR superfamily, and considering the wide variety of biological activities exhibited by proteins in that superfamily, one skilled in the art would not unquestioningly accept assertions regarding an unproven biological activity for a new member of the superfamily. For claims 23, 24, 26-29, 35, and 36, these claims do not require any functional activity, and the specification does not teach how to use proteins with no functional activity. For claims 30-34, 37, and 38, the claims encompass variants with undisclosed biological activities, and it is not clear how to make or use a protein which has an undisclosed biological activity. Considering the limited teachings in the specification, and the unpredictability of biological activity for members of the TNFR superfamily, it is maintained that the specification is enabling only for variants which exhibit the disclosed biological activity of interfering with the ability of LIGHT/TANGO-69, LT.alpha., or HSV gD to bind mHVEM.

Claims 24, 25, and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims require access to the ATCC deposited plasmid recited in the claims. As a required element the plasmid must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the specifically deposited plasmid, and it does not appear to be readily available material.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 30-34, 37, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Spear et al US 6,303,336. Spear teaches a polypeptide which is soluble and comprises a sequence 92.5% identical to SEQ ID NO:18. See Figure 8A, SEQ ID NO:7, and claims 5-8, 23-26. See also the attached alignment of SEQ ID NO:18 ("QY") with Spear SEQ ID NO: 7 ("DB") The polypeptide lacks the transmembrane and cytoplasmic domains, and is fused to a heterologous Fc fragment. Although the reference is silent upon "TANGO-69-receptor activity", this would reasonably appear to be an inherent property of the protein.

Claims 30-34, 37, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Montgomery et al (Cell 87:427-436, 1996). Montgomery teaches the same fusion protein as Spear et al 6,303,336, and further teaches that the fusion protein blocks herpesvirus infection, indicating that the fusion protein exhibits a "TANGO-69-receptor activity." The reference protein therefore clearly meets each and every limitation of these claims.

Allowable Subject Matter

SEQ ID NO:18 is free of the art, as the prior art does not teach or suggest the C-terminal sequence which differs from HVEM. Prior art teaching HVEM sequences, variants, and synonyms include Montgomery et al (Cell 87:427-436, 1996), Spear et al (US 6,303,336), Ni et al (TR2; WO 98/18824), Terry-Allison et al (HveA, Journal of Virology 72(7): 5802-5810) and Hsu et al (ATAR, Journal of Biological Chemistry 272: 13471-13474, 1997).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone numbers for this Group are now (703) 872-9306 for Before Final responses, and (703) 872-9307 for After Final responses. Faxes for this Group can also be sent to (708) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 22, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600

RESULT 5
US-08-509-024-7
; Sequence 7, Application US/08509024B
; Patent No. 6291207
; GENERAL INFORMATION:
; APPLICANT: SPEAR, Patricia G.
; APPLICANT: MONTGOMERY, Rebecca I.
; TITLE OF INVENTION: HERPES VIRUS ENTRY RECEPTOR PROTEIN
; FILE REFERENCE: 0290-1
; CURRENT APPLICATION NUMBER: US/08/509,024B
; CURRENT FILING DATE: 1995-07-25
; NUMBER OF SEQ ID NOS: 7
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 7
; LENGTH: 419
; TYPE: PRT
; ORGANISM: Homo sapiens
US-08-509-024-7

Query Match 92.5%; Score 1060; DB 4; Length 419;
Best Local Similarity 97.9%; Pred. No. 1.2e-87;
Matches 184; Conservative 0; Mismatches 4; Indels 0; Gaps 0;

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Qy       1 MEPPGDWGPPPWRSTPRTDVLRLVLYLTFLGAPCYAPALPSCKEDEYPVGSECCPKCSPG 60
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Db       1 MEPPGDWGPPPWRSTPRTDVLRLVLYLTFLGAPCYAPALPSCKEDEYPVGSECCPKCSPG 60

Qy      61 YRVKEACGELTGTVCEPCPPGTYIAHLNGLSKCLQCQMCDPAMGLRASRNCSRTENAVCG 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 YRVKEACGELTGTVCEPCPPGTYIAHLNGLSKCLQCQMCDPAMGLRASRNCSRTENAVCG 120

Qy     121 CSPGHFCIVQDGDHCAACRAYATSSPGQRVQKGGTESQDTLCQNCPPGTFSPNGTLEECQ 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 CSPGHFCIVQDGDHCAACRAYATSSPGQRVQKGGTESQDTLCQNCPPGTFSPNGTLEECQ 180

Qy     181 HQTNWPNH 188
           |||    |
Db     181 HQTKCRIH 188
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